Sleep and Aging

Richard P. Millman, MD

As one ages, one frequently complains of sleep not being restorative. It is a total myth that one needs less sleep after age 65 and in fact, there is really minimal change in sleep period time, the amount of time one stays in bed, with aging. There is a gradual decrease in total sleep time of approximately 27 minutes per decade from mid-life until the eighth decade. What does happen with aging is that sleep becomes much more fragmented. There is also a decrease in stage N-3 or slow wave sleep from young adulthood to middle age without a significant change after age 50. This stage of sleep is a stage where growth hormone is produced and the relative drop in slow wave sleep with increasing age may account for some of the shrinkage we see in the elderly. There are multiple problems that occur at any age range. Some of them are enhanced with aging and these sleep problems will be discussed in further detail.

Circadian Rhythm Issues

Studies have shown that external cues and activity are most important in keeping elderly patients awake during the daytime and asleep at night. In demented nursing home patients, sleep monitoring has demonstrated that these patients may totally lose the normal bedtime and wakeup times seen in healthy elderly individuals. In fact, demented individuals who are not stimulated may sleep part of every hour of a 24 hour day.

In regards to circadian rhythm, many older individuals maintain a regular bedtime and wakeup time. Sometimes lonely or depressed individuals will tend to go to bed earlier and then wake up in the middle of the night with the chief complaint of insomnia. This behavior is consistent with an advanced sleep phase syndrome and is relatively easy to treat. It is important to have the patient increase their activities in the late afternoon and early evening and slowly push their bedtime later at 15 minute intervals.

Other individuals do not fall asleep until 2 or 3 am and then get up at 11 am. Although this picture of delayed phase syndrome has been classically described in adolescent and young adults, it also can be seen in older populations. The key feature is that once the patient falls asleep, they stay asleep until the morning. Patients may complain of initiation insomnia or excessive daytime sleepiness, especially if they force themselves to get up at 7 – 8 am. With the delayed phase syndrome, having a patient try to go to bed earlier absolutely does not work and, in fact, may increase complaints of initiation insomnia. Sedative hypnotics are not effective though perhaps evening melatonin may help reset the circadian clock in select individuals. Another option is to have the patient undergo therapy with bright light exposure in the morning.

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Insomnia

The definition of insomnia is difficulty falling asleep, difficulty maintaining sleep or perception of poor quality sleep. This has to result in problems with daytime functioning including mood changes and fatigue. Chronic insomnia has been shown in multiple studies to occur in approximately 10 – 15% of the population. Chronic insomnia is associated with poor physical and emotional health. It has also been shown to precede the onset of depression in multiple studies. The earliest of this was a study done by Ford and Kamerow.[1] They demonstrated that the odds ratio of developing depression in the year after a bout of insomnia was markedly elevated at 39.8. If the insomnia resolved, the odds ratio was 1.6. This implies that there should be aggressive treatment of insomnia when it first occurs. In fact, patients become chronic insomniacs after as little as three to four weeks of not being able to sleep.

Clearly, any medications may not only cause insomnia but cause daytime sleepiness. In fact, withdrawal of certain medications may lead to insomnia or daytime sleepiness. It is therefore very important that the clinician look at all medication changes when assessing sleep problems. In addition, certain medications (such as fluoxetine) can be stimulating. If a patient takes that specific medication in the evening it may keep cause insomnia; this medication should clearly be given in the morning.

In regards to medical causes, heart failure, asthma exacerbations, COPD, sleep apnea and nasal congestion can all cause the patient to have insomnia and it is important to treat the underlying conditions. Pain certainly can cause insomnia and insomnia can increase chronic pain and headaches. Frequently in these patients it is important not only to treat the insomnia but also treat the underlying condition. Insomnia is clearly associated with psychiatric disorders and most psychiatric disorders including mood issues, anxiety and substance abuse all have either daytime sleepiness or insomnia associated with them. Since insomnia can make depression worse and depression can make insomnia worse, it is not unreasonable to treat both conditions when a patient presents. As noted above, circadian rhythm disorders can present as insomnia. Patients can also have primary or psycho-physiological insomnia. This is basically a learned condition in which patients really have lost the capabilities of sleeping.

Patients can be treated behaviorally. As shown in table there are very simple sleep hygiene education rules that all patients should use. More aggressive behavioral therapy can also be performed using cognitive behavioral therapy.[2] Cognitive behavioral therapy may include a combination of sleep restriction, stimulus control and relaxation therapy. It does require the patient to follow instructions very carefully if they want to have a successful result.

In regards to medications, frequently sedative hypnotic agents can have side effects, especially in the elderly. Long acting benzodiazepine agents such as diazepam,

Table 1. Sleep Hygiene Education

- Maintain a regular schedule for going to bed and arising
- Avoid excessive time in bed
- Avoid taking naps during the day and early evening
- Use the bed only for sleeping and sexual relations
- Do not watch the clock while in bed
- Do something relaxing before bedtime
- Avoid light exposure from computers and phones prior to bedtime
- Make the bedroom as quiet and comfortable as possible
- Avoid taking the troubles of the day to bed
- Avoid consumption of alcohol or caffeinated beverages, especially within 6 hours of bedtime
- Get exercise, but early in the day (not within two hours of bedtime)
- Avoid going to bed hungry - eat a light snack in the evening if necessary
- Avoid bright light exposure in the hour before bedtime

flurazepam, and chloradiazepoxide have been associated with an increased risk of hip fractures.[3] Long-acting antihistamines, such as diphenhydramine, have also been demonstrated to cause cognitive function abnormalities and should also not be used in the elderly.[4] On the other hand untreated insomnia has in itself been associated with an increase in injuries due to falls.

Medications are clearly indicated in patients who fail behavioral therapies. Medications are also indicated when there are coexistent co-morbidities such as chronic headaches, chronic pain or psychiatric disorders. In the later situation the co-morbid condition makes the insomnia worse and vice versa. The question then arises about what agent to use. The basic concept in using sedatives is to have the patient take the drug in the evening and make sure that the effects are gone in the morning. One runs into potential problems with any of the shorter acting benzodiazepines since they are potentially addictive. The non-benzodiazepine agents working at the GABA receptor, such as zaleplon, zolpidem and eszoplicone, may be more appropriate. The only agent that has been to be safe if somebody cannot fall asleep for several hours or wakes up in the middle of the night and cannot fall back asleep is zaleplon.[5] Sedating anti-depressive agents such as trazodone and mirtazepine might be very helpful in this age range as well. The latter drug also increases appetite and may be beneficial in elderly patients who have trouble keeping weight on.

Restless Legs Syndrome

Restless legs syndrome (RLS) is a syndrome in which there is an incredible desire to move one's limbs; usually associated with pain or paresthesias. This is basically a sensation of restlessness which occurs when the patient is awake. The symptoms are worse at rest and resolve once the afflicted individual starts walking around. RLS seems to have a circadian rhythm and symptoms are worse in the evening or at night. RLS can be associated with **periodic limb movements during sleep (PLMS)**. RLS increases in frequency with aging and does need to be treated if there is significant discomfort or insomnia. PLMS should be treated if there is associated sleep fragmentation and complaints of insomnia or excessive daytime sleepiness.[6]

The basic mechanism behind the development of RLS as well as PLMS is a relative decrease in dopamine. One of the first things that a clinician should do is to check a serum ferritin level. It turns out that iron is associated with dopamine production. If the ferritin level is under 50mg/ml then it is worthwhile to give the patient supplemental iron even if the patient is not grossly anemic. Frequently iron therapy alleviates RLS symptoms. Dopaminergic agents such as pramipexole and ropinirole have been approved by the FDA as treatments for restless legs. Other agents that have been used include opioids, gabapentin and carbamazepine. There is really no role for benzodiazepines in treatment of either restless legs or periodic limb movement even though these agents historically were the first drugs used for this condition.

REM Sleep Behavior Disorder

Generally in REM sleep, the brain is incredibly active and this activity causes vivid dreaming. As opposed to cats and dogs that demonstrate twitching of the extremities in REM sleep, humans have no muscle tone which basically prevents them from acting out a dream. The only muscles that are effectively working are the eye muscles and the diaphragm. In patients with REM sleep behavior disorder, the switch that turns off muscle activity during REM sleep is dysfunctional and patients actually have at times muscle activity allowing them to act out their dreams. One can make the diagnosis of REM sleep behavioral disorder if REM sleep with increased muscle tone is observed on polysomnography. This observation has to be associated with at least one of the following: 1) a history of sleep related injuries or disruptive behavior associated with dream enactment. 2) Abnormal REM sleep behavior documented during the actual sleep study.[7]

REM sleep disorder can be idiopathic. It typically will occur with increased age and in men more than women. Unfortunately, some patients with idiopathic REM sleep behavior disorder may develop neurodegenerative disorders such as Parkinson's disease or Lewi body dementia.[8] REM sleep behavior disorder may occur in association with various neurological conditions including brain stem vascular lesions, brain stem neoplasms, demyelinating disease, auto-immune inflammatory disorders and neurodegenerative disorders. It may be triggered by medications as well.

The basic tenant of treating REM sleep behavior disorders is to protect the patient from injury. Benzodiazepines, such as clonazepam, have been shown to be effective in treating the disorder. In some patients this drug may last too long in the patient's system and those patients with daytime impairment from the medication might do better with a shorter acting agent such as lorazapam. Patents who have co-existing snoring or sleep apnea could potentially develop worse sleep apnea when given a benzodiazepine, so it is always important to do a sleep study on patients with suspected REM sleep behavior disorder not only to make the diagnosis of the disorder, but also to make sure the patient does not have sleep apnea. There are recent data suggesting

that melatonin at the beginning of the night may improve some patients.[9]

Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) is a syndrome where the throat relaxes and closes off at night. When a patient goes to sleep, the majority of the pharyngeal muscles relax and the normal vacuum that one creates during inspiration pulls the throat closed. An obstructive apnea is an event lasting ten seconds or longer where the pharynx is totally closed off. A hypopnea is an episode where the throat is nearly closed off but there is still some minimal airflow. There is significant impedance to airflow such that the oxygen saturation falls at least 4% or more. More recently, **respiratory effort related arousals (RERAs)** have been described. These are events where the throat is narrowed, there is increased inspiratory effort and snoring typically persists until there is an arousal from sleep and the throat is able to open again. In those patients, there is not significant O2 desaturation. The pharynx may collapse at the region of the uvula and soft palate or in the hypopharynx or at both locations.

OSA is associated with not only sleep fragmentation, but also hypoxemia and hypercapnia. As a result, there can be excessive daytime sleepiness as well as sleep disruption. Nocturia can be a frequent symptom in patients with sleep apnea. The increase in negative suction that develops in the thorax as a patient tries to inhale against a closed glottis increases the return of fluids into the heart. Dilatation of the right atrium leads to an increase in atrial natriuretic peptide production. This leads to increased stimulus for the patient to urinate and nocturia. Often patients think that they will not be able to use positive pressure therapy during the night because they go to the bathroom frequently. Typically this symptom disappears when a patient is put on positive pressure therapy.

Obstructive events at night lead to falls in oxygen level and increase in carbon dioxide levels. When the patient wakes up there is catecholamine release and a surge in blood pressure. Catecholamine levels have been noted to elevated during the daytime and there is increasing evidence that obstructive sleep apnea can be a cause of daytime hypertension. Sleep apnea, however, may not be a contributing factor to daytime hypertension in patients over 60 because they have already developed fixed changes in their vasculature.[10]

OSA has been associated with an increase in cerebral vascular accidents while sleeping as well as myocardial infarctions. There is also increasing data showing that OSA is a contributing factor to atrial fibrillation. In fact, patients with untreated OSA and atrial fibrillation, have a higher chance of cardioversion failure than those patients where the sleep apnea is treated.[11]

Patients with OSA can have mood issues and more easily fall asleep during the daytime. The real fear in the elderly is that they could potentially fall asleep while driving a motor vehicle. Sleep apnea can also cause micro-sleeps, leading to inattentiveness while driving.

Risk factors for sleep apnea include upper body obesity, a family history of sleep apnea, nasal obstruction, retrognathia or pharyngeal narrowing. The latter can be caused by a deep set palate, an elongated uvula or enlarged tonsils. Age appears to be an independent factor for developing sleep apnea and there has been some discussion whether one should use a cutoff of five episodes of apnea/hypopnea per hour as the true level of significant level of sleep apnea in the elderly.

The treatment of sleep apnea in the elderly has some of the same premises as in younger populations. Clearly, in overweight individuals, weight loss is important. Alcohol and benzodiazepines in the evening can also cause the pharynx to collapse more readily and should be avoided. If the nose is congested, medications can be used to open up the nose. In the dry wintertime, saline nasal spray would be helpful as well. Some patient may do well using nasal strips to keep the nose open at night. The mainstay of treatment is positive airway pressure. If an elderly patient has mild to moderate sleep apnea and cannot tolerate positive pressure therapy, than one can consider an adjustable oral appliance.

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Richard P. Millman, MD, is Professor of Medicine & Pediatrics and Vice Chairman of Medicine at the Warren Alpert Medical School of Brown University, and Medical Director of the Sleep Disorders Center of Lifespan Hospitals.

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Discussion of off-label usage: Trazodone and mirtazepine. Clonazepam, lorazapam and melatonin for REM sleep behavior disorder.

Correspondence

Richard P. Millman, MD
APC 701
Rhode Island Hospital
593 Eddy Street
Providence, RI 02903
phone: (401) 444-2670
fax: (401) 444-8447
e-mail: rmillman@lifespan.org